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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,500	03/29/2002	Nobuo Hanai	249-255	9448

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 08/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,500	HANAI ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,9-13,15,16,20-28,30-32,36-41,48,50,51,55-58 and 62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,9-13,15,16,20-28,30-32,36-41,48,50,51,55-58 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/13/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibit A*.

DETAILED ACTION

1. Claims 3-5, 7-8, 14, 17-19, 25, 29, 33-35, 42-47, 49, 52-54, 59-61 and 63-66 are cancelled.

Claims 1-2, 6, 9-13, 15-16, 20-24, 48, 51, 55-58 have been amended.

2. Claims 1-2, 6, 9-13, 15-16, 20-28, 30-32, 36-41, 48, 50-51, 55-58 and 62 are under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains New Grounds of Rejections.

Restriction/Election

5. Applicant requests reconsideration of the restriction requirement in so far as claim 62 was included in Group II of the restriction requirement mailed 7/9/2004 and claim 62 should be included in the elected invention of Group I, especially in light of the Examiner's comments on pages 8-11 of the previous Office Action mailed 1/13/2005. Upon further consideration, and in view of Applicant's request, the restriction requirement between claim 62 and the elected invention of Group I is hereby WITHDRAWN. Thus, claim 62 is currently under examination with the elected invention of Group I

Objections/Rejections Withdrawn

6. The objection to Figure 14 and 32 for not containing labels is withdrawn in view of the drawings filed 7/13/2005.

7. The objections to claim 63 as being dependent upon a withdrawn claim is withdrawn in view of the cancellation of the claim.

8. The rejection of claims 1-9, 14-19, 24-25, 29, 33-35 and 64-66 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation of "derivative" is withdrawn in view of the amendments to the claims.

9. The rejection of claims 1-41, 48-58 and 63-66 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation of "ganglioside GD3 which is conjugated..." is withdrawn in view of the amendments to the claims.

10. The rejection of claim 14 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation of "comprises CDR of an H chain V region and an L chain V region" is withdrawn in view of the cancellation of the claim.

11. The rejection of claims 63-66 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation of "the human CDR grafted antibody and the antibody fragment thereof" is withdrawn in view of the cancellation of the claims.

12. The rejection of claim 7 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation of "the humanized antibody is a human chimeric antibody" is withdrawn in view of the cancellation to the claim.

13. The rejection of claims 7, 48 and 63-66 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation of "human-CDR grafted antibody" is withdrawn in view of the amendments to the claims.

14. The rejection of claims 1-41, 48-58 and 63-66 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation of "reacts" is withdrawn in view of the amendments to the claims.

15. The rejection of claims 6, 13 and 23 under 35 U.S.C. 112, first paragraph for lack of enablement is withdrawn in view of applicant's successful completion of the deposit requirements. In view of this a deposit rejection of claim 62, not previously examined is obviated.

16. The rejection of claims 1-2 and 64-66 under 35 U.S.C 102(b) as being anticipated by Chapman et al is withdrawn in view of the amendments to the claims.

17. The rejection of claims 1-2, 7-9, 14-16, 24-25, 36-37, 48-51 and 63-66 under 35 U.S.C. 103(a) as being unpatentable over Chapman et al in view of Queen et al and LeBerthon et al is withdrawn in view of the amendments to the claims.

18. The rejection of claims 1-19, 24-29, 33-39, 48-54 and 63-66 under 35 U.S.C. 103(a) as being unpatentable over Hanai et al as evidenced by Shitara et al [c] in view of Queen et al and Nakamura et al is withdrawn in view of the certified translations of foreign priority documents Japan 11/278291 filed 9/30/1999 and Japan 2000/105088 filed 4/6/2000 which provide adequate written description for the claimed subject matter. Thus, The filing date of the present claims is deemed to be 9/30/1999 and Hanai et al no longer qualifies as prior art.

19. The rejection of claims 3-5, 7-8, 14, 17-19, 25, 29, 33-35, 48-49, 52-54 and 63-66 under 35 U.S.C. 103(a) as being unpatentable over Shitara et al [a] in view of Queen et al and Nakamura et al is withdrawn in view of the cancellation of the claims and the amendments to claim 48.

20. The rejection of claims 3-5, 7-8, 14, 17-19, 25, 29, 33-35, 48-49, 52-54 and 63-66 under 35 U.S.C. 103(a) as being unpatentable over Shitara et al [b] in view of Queen et al and Nakamura et al is withdrawn in view of the cancellation of the claims and the amendments to claim 48.

21. The rejection of claims 3-5, 7-8, 14, 17-19, 25, 29, 33-35, 48-49, 52-54 and 63-66 under 35 U.S.C. 103(a) as being unpatentable over Hanai et al as evidenced by Shitara et al [c] in view of Queen et al and Nakamura et al is withdrawn in view of the cancellation of the claims and the amendments to claim 48.

22. The rejection of claims 3-5, 7-8, 14, 17-19, 25, 29, 33-35, 48-49, 52-54 and 63-66 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of US Patent No.6,437,098 B1 in view of Queen et al and Nakamura et al is withdrawn in view of the cancellation of the claims and the amendments to claim 48.

23. The rejection of claims 3-5, 7-8, 14, 17-19, 25, 29, 33-35, 48-49, 52-54 and 63-66 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of US Patent No. 5,750,078 in view of Shitara et al [c] and Queen et al and Nakamura et al is withdrawn in view of the cancellation of the claims and the amendments to claim 48.

24. The rejection of claims 3-5, 7-8, 14, 17-19, 25, 29, 33-35, 48-49, 52-54 and 63-66 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of US Patent No. 6,495,666 B2 in view of Shitara et al [c] and Queen et al and Nakamura et al is withdrawn in view of the cancellation of the claims and the amendments to claim 48.

Response to Arguments

25. The rejection of claims 10-13, 20-23, 26-28, 30-32 and 36-41 under 35 U.S.C. 112, second paragraph as being indefinite in the recitation of "derivative" is maintained.

The response filed 7/13/2005 has been carefully considered, but is deemed not to be persuasive. The response states that the amendments obviate this rejection. In response to this argument, it is respectfully pointed out that claims 10-13, 20-23, 26-28, 30-32 and 36-41 still recite the term "derivative" and therefore, the rejection is maintained for reasons already of record.

26. The rejection of claim 24 under 35 U.S.C. 112, first paragraph for lack of enablement is maintained.

The response filed 7/13/2005 states that this rejection is obviated in view of the amendments to the claims, which have been amended to recite that the peptide comprises CDR1, CDR2 and CDR3 of the heavy chain variable region and CDR1, CDR2 and CDR3 of the light chain variable region. In response to this argument and in view of the amendments to the claim, it is unclear whether a peptide would have all six

CDRs in the context of the frameworks and have the required binding function because a peptide is defined as a short amino acid sequence of about 2 to about 50 amino acids (see Exhibit A attached to the back of this Office Action) and as such a "peptide" would not contain the CDRs in the context of the frameworks and would not bind antigen. It is reiterated that applicant is enabled for an antibody or antigen-binding fragment thereof comprising all six CDRs, three from the heavy chain and three from the light chain, wherein the antibody or antigen-binding fragment thereof binds antigen.

27. The rejection of claims 1-2, 6, 9-13, 15-16, 24, 26-28, 36-39 and 50-51 under 35 U.S.C. 103(a) as being unpatentable over Shitara et al [a] in view of Queen et al and Nakamura et al is maintained.

The response filed 7/13/2005 has been carefully considered, but is deemed not to be persuasive. The response argues that it was not predictable from the cited art that an antibody conjugate of KM871, for example, would retain the antibody properties of the original unconjugated antibody. Applicant cites Presentini et al and points to the last three lines of page 309, which states that a conjugate must meet certain criteria of sensitivity, specificity and stability, meaning that it must be shown when an antibody conjugate is produced, that the antigen binding activity and antigen specificity of the antibody conjugate must be examined. In response to this argument, the art of Presentini et al is with respect to analytical immunochemical detection, however, the instantly claimed immunoconjugate is for immunotherapy. It is unclear how the need to test an immunoconjugate renders the claimed invention nonobvious, since the need to

test does not show a lack of motivation or lack of a reasonable expectation of success. Applicant argues against Nakamura et al of the instant rejection, which applicant argues that the binding activity of the radioisotope-antibody conjugate is 90-100% of the original antibody, whereas the radioisotope-antibody-IL2 conjugate has 10-40% lowered binding activity. Applicant argues that the presently claimed antibody conjugate retains the antigen binding activity and specificity of the unconjugated antibody and showed increased cytotoxic activity and provided a greater anti-tumor effect and greater life-prolonging effect *in vivo* compared to the administration of the anti-GD3 chimeric antibody alone or in combination with IL-2. Applicant concludes that these properties would not have been expected from the references cited in the rejection. In response to these arguments, while it is true that Table 1 of Nakamura et al does show that the radioisotope-antibody-IL-2 conjugate has lowered binding activity relative to the radioisotope-antibody conjugate, this is insufficient evidence showing that there was no reasonable expectation of success to support a conclusion of nonobviousness (MPEP 2143.02). Additionally, Nakamura et al show that for the radioisotope-antibody conjugate, the tumor received 13% of the radioisotope, whereas the radioisotope-antibody-IL2 conjugate in the words of Nakamura et al "demonstrated significantly higher tumor uptake (19%)" of the radioisotope, which increased to 46% at day 3 (see Figure 1 and text at page 2652) and the radioisotope-antibody-IL2 conjugate demonstrated a higher tumor to nontumor ratio compared to the radioisotope-antibody conjugate (see Figure 4). Thus, despite a small decrease in binding activity of the antibody-IL2 conjugate, Nakamura et al provide a detailed enabling methodology, a

motivation to produce the presently claimed antibody-IL2 conjugate and evidence that the claimed invention would be successful. Therefore, one of ordinary skill in the art at the time then invention was made would have been motivated and expected enhanced cytotoxicity and greater anti-tumor effect of the presently claimed antibody-IL-2 conjugate in view of the combined teachings of Shitara et al [a] in view of Queen et al and Nakamura et al. Further, applicant is reminded that all that is required is a reasonable expectation of success, not absolute predictability of success. See *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

Therefore, the rejection is maintained.

28. The rejection of claims 1-2, 6, 9-13, 15-16, 24, 26-28, 36-39 and 50-51 under 35 U.S.C. 103(a) as being unpatentable over Shitara et al [b] in view of Queen et al and Nakamura et al is maintained.

The response filed 7/13/2005 has been carefully considered, but is deemed not to be persuasive. The response argues as above for Shitara et al [a] in view of Queen et al and Nakamura et al and the examiners response to these arguments above applies here as well.

29. The rejection of claims 1-2, 6, 9-13, 15-16, 24, 26-28, 36-39 and 50-51 under 35 U.S.C. 103(a) as being unpatentable over Shitara et al [c] in view of Queen et al and Nakamura et al is maintained.

The response filed 7/13/2005 has been carefully considered, but is deemed not to be persuasive. The response argues as above for Shitara et al [a] in view of Queen et al and Nakamura et al and the examiners response to these arguments above applies here as well.

30. The rejection of claims 1-2, 6, 9-13, 15-16, 24, 26-28, 36-39 and 50-51 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of US Patent No.6,437,098 B1 in view of Queen et al and Nakamura et al is maintained.

The response filed 7/13/2005 has been carefully considered, but is deemed not to be persuasive. The response requests the examiner to hold this rejection in abeyance until allowable subject matter is identified and applicant will consider filing a terminal Disclaimer at that time. The response also states that the present application and the claims of US Patent No. 6,437,098 were commonly owned at the time of the invention of this application. In response to these arguments, no Terminal disclaimer has been filed and the rejection is maintained.

31. The rejection of claims 1-2, 6, 9-13, 15-16, 24, 26-28, 36-39 and 50-51 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of US Patent No. 5,750,078 in view of Shitara et al [c] and Queen et al and Nakamura et al is maintained.

The response filed 7/13/2005 has been carefully considered, but is deemed not to be persuasive. The response requests the examiner to hold this rejection in abeyance until allowable subject matter is identified and applicant will consider filing a terminal Disclaimer at that time. The response also states that the present application and the claims of US Patent No. 5,750,078 were commonly owned at the time of the invention of this application. In response to these arguments, no Terminal disclaimer has been filed and the rejection is maintained.

32. The rejection of claims 1-2, 6, 9-13, 15-16, 24, 26-28, 36-39 and 50-51 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of US Patent No. 6,495,666 B2 in view of Shitara et al [c] and Queen et al and Nakamura et al is maintained.

The response filed 7/13/2005 has been carefully considered, but is deemed not to be persuasive. The response requests the examiner to hold this rejection in abeyance until allowable subject matter is identified and applicant will consider filing a terminal Disclaimer at that time. The response also states that the present application and the claims of US Patent No. 6,495,666 B2 were commonly owned at the time of the invention of this application. In response to these arguments, no Terminal disclaimer has been filed and the rejection is maintained.

New Grounds of Objections/Rejections

33. Claims 10-13, 20-23, 26-28, 30-32, 36-41, 50, 55-58 and 62 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 10-13, 20-23, 26-28, 30-32 and 36-41 are indefinite for reciting "The derivative". There is insufficient antecedent basis for this limitation. Base claims 1 and 2 from which claims 10-13, 20-23, 26-28, 30-32 and 36-41 depend do not recite any "derivative".

b. Claims 50, 55-58 and 62 indefinite for reciting "The human CDR grafted antibody". There is insufficient antecedent basis for this limitation. Base claim 48 from which claims 50, 55-58 and 62 depend does not recite a "human CDR grafted antibody".

c. Claim 24 is indefinite in the recitation of "a peptide comprising CDR1, CDR2 and CDR3 of the H chain V region and CDR1, CDR2 and CDR3 of the L chain V region." A peptide is defined in the art as a molecule consisting of about 2 to about 50 amino acids in length (see Exhibit A attached to the back of this Office Action). Does the "peptide" only comprise the recited CDRs or does the claimed "peptide" also comprise the frameworks, which would make it a polypeptide rather than a peptide?

34. Claim 48 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

The response filed 7/13/2005 has introduced NEW MATTER into claim 48. Presently amended claim 48 recites that the humanized anti-GD3 antibody comprises the heavy chain variable region of SEQ ID NO:9 having at least one amino acid residue selected from amino acid residue 10, 11, 20, 28, 84, 91, 95, 97 and 115 of SEQ ID NO:9 replaced by another amino acid residue and comprises the light chain variable region of SEQ ID NO:10 having at least one amino acid residue selected form amino acid residues 49, 65 and 71 of SE ID NO:10 replaced with another amino acid residue. The response did not point out where support for newly added claim 54 could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). Upon review by the Examiner, the specification at page 61 discloses a humanized anti-GD3 antibody comprising the heavy chain variable region of SEQ ID NO:9 wherein amino acid residues 10, 11, 20, 28, 84, 91, 95, 97 and 115 of SEQ ID NO:9 are replaced with the corresponding murine KM641 amino acid residues Asp, Phe, Val, Ala, Arg, Ser, Phe, Thr, and Leu, respectively, and comprises the light chain variable region of SEQ ID NO:10 wherein amino acid residues 49, 65 and 71 are replaced with the corresponding murine KM641

amino acids Tyr, Ser and Phe, respectively. Thus, the specification does not provide adequate written support for the broader limitations of the present claims, wherein the recited amino acid positions of SEQ ID Nos:9 and 10 are replaced with just any amino acid and wherein only one, or only two amino acids (i.e., "at least one") of the heavy and light chain variable regions are replaced with just any amino acid as well as various combinations of heavy and light chain amino acid substitutions as encompassed by the presently amended claim. As presently, amended claim 48 now recites limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in presently amended claim 48, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claim 48 in the specification or claims, as filed, or remove these limitations from the claim in response to this Office Action.

35. Claim 48 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a humanized anti-GD3 antibody comprising the heavy chain variable region of SEQ ID NO:9 wherein amino acid residues 10, 11, 20, 28, 84, 91, 95, 97 and 115 of SEQ ID NO:9 are replaced with amino acid residues Asp, Phe, Val, Ala, Arg, Ser, Phe, Thr, and Leu, respectively, and comprising the light chain variable region of SEQ ID NO:10 wherein amino acid residues 49, 65 and 71 are replaced with amino acids Tyr, Ser and Phe, respectively, does not reasonably provide

enablement for a humanized anti-GD3 antibody comprising the heavy chain variable region of SEQ ID NO:9 wherein at least one of amino acid residues 10, 11, 20, 28, 84, 91, 95, 97 and 115 of SEQ ID NO:9 is/are replaced with another amino acid residue, and comprising the light chain variable region of SQE ID NO:10 wherein at least one of amino acid residues 49, 65 and 71 is/are replaced with another amino acid residue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the presently claimed invention is drawn to humanized anti-GD3 antibodies. Claim 48 is broadly drawn to a humanized anti-GD3 antibodies comprising the heavy chain variable region of SEQ ID NO:9 wherein at least one of amino acid residues 10, 11, 20, 28, 84, 91, 95, 97 and 115 of SEQ ID NO:9 is/are replaced with another amino acid residue, and comprising the light chain variable region of SEQ ID NO:10 wherein at least one of amino acid residues 49, 65 and 71 is/are replaced with another amino acid residue. Thus, the claims broadly encompass framework amino

acid substitutions wherein the amino acids are not selected from the frameworks of murine KM641 (CDR donor antibody) as well as non-conservative amino acid substitutions at the recited framework positions in the humanized GD3 antibody.

The specification teaches a humanized anti-GD3 antibody comprising the heavy chain variable region of SEQ ID NO:9 wherein amino acid residues 10, 11, 20, 28, 84, 91, 95, 97 and 115 of SEQ ID NO:9 are replaced with murine KM641 amino acid residues Asp, Phe, Val, Ala, Arg, Ser, Phe, Thr, and Leu, respectively, and comprising the light chain variable region of SQE ID NO:10 wherein amino acid residues 49, 65 and 71 are replaced with murine KM641 amino acids Tyr, Ser and Phe, respectively. The specification does not teach a humanized anti-GD3 antibody comprising just any amino acid substitution at the recited amino acid positions of SEQ ID Nos:9 and 10 or at least one of the recited amino acid positions of SEQ ID Nos:9 and 10 and wherein the humanized antibody preserves the GD3 binding specificity of the parental antibody. There is no exemplary guidance in applicant's specification of an anti-GD3 humanized antibody wherein only one of amino acid residues 10, 11, 20, 28, 84, 91, 95, 97 and 115 of SEQ ID NO:9 is replaced and wherein only one of amino acid residues 49, 65 and 71 of SEQ ID NO:10 is replaced or combinations thereof wherein at least one of amino acid residues 10, 11, 20, 28, 84, 91, 95, 97 and 115 of SEQ ID NO:9 are replaced and wherein at least one of amino acid residues 49, 65 and 71 of SEQ ID NO:10 are replaced and wherein the humanized antibody retains the GD3 binding activity of the parental antibody.

It is well established in the art that simple CDR grafting, wherein the transfer of the six CDRs of a non-human antibody onto human framework regions often produces inactive molecules and additional rounds of mutagenesis are required to confer to the recombinant molecule the same specificity of the CDR-donor antibody. Adair et al (WO 91/09967) teach that for antibody humanization non-human CDRs are transferred onto the most highly homologous human frameworks and require the additional transfer of specific sets of framework residues from the non-human antibody which also contributes the CDRs (see pages 17-23 and Examples). Thus, it is unclear if the recited anti-GD3 humanized antibody which may comprise only one heavy chain amino acid framework substitution and only one light chain framework amino acid substitution would have the required GD3 binding function. It is unlikely that a humanized antibody as defined by the claim, which contains just any amino acid substituted at the recited framework position(s) and combinations thereof would have the required GD3 binding activity. Applicants have provided insufficient evidence or nexus that would lead the skilled artisan to predict the ability of using a humanized antibody containing any combination of amino acid substitutions in the recited heavy and light chain framework positions, resulting in a humanized antibody that retains the antigen specificity of the parental non-human antibody. One of skill in the art would neither expect nor predict the appropriate functioning of the humanized antibody as broadly as is claimed.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to using the

GD3 humanized antibody containing at least one amino acid substitution at amino acid residues 10, 11, 20, 28, 84, 91, 95, 97 and 115 of SEQ ID NO:9 and at least one amino acid substitution at amino acid residues 49, 65 and 71 of SEQ ID NO:10. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Conclusion

36. No claim is allowed.

37. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

38. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571)

272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to Tony Parks for Art Unit 1643 whose telephone number is 571-272-0543.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

close window

Exhibit A

AD-250X250

Source: http://www.medterms.com
MedTerms is the Medical Dictionary of MedicineNet.com

Definition of Peptide

Peptide: A molecule consisting of 2 or more amino acids. Peptides are smaller than proteins, which are also chains of amino acids. Molecules small enough to be synthesized from the constituent amino acids are, by convention, called peptides rather than proteins. The dividing line is at about 50 amino acids. Depending on the number of amino acids, peptides are called dipeptides, tripeptides, tetrapeptides, and so on.

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